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Risk assessment of sydney classification categories in lymph node aspiration smears

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Abstract

Aim: We aimed to evaluate risk categorization according to the Sydney classification in lymph node aspirations performed in our hospital, which has a large archive.

Material and Methods: Three hundred fifteen lymph node fine-needle aspiration (FNAB) smears were reassessed and classified using the Sydney classification. Clinical and histopathological findings were compared. Risk of malignancy (ROM), sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were evaluated.

Results: Fine needle aspiration biopsies (FNAB) of a total of 315 cases, 74 (23.5%) men and 241 (76.5%) women, were examined. One hundred sixty-eight of 315 cases had a history of previously diagnosed tumors. In terms of diagnostic categories, 12 (3.8%) cases were L1 (non-diagnostic), 122 (38.7%) L2 (benign), 7 (2.2%) L3 (AUS/ALUS), 27 (8.6%) L4 (suspicion of malignancy), and 147 (46.7%) were in the L5 (malignant) category. Thus, L5 and L2 were the most frequently used categories. There was discordance in the histopathologic examination of 25 (20,5%) cases (mostly Hodgkin's lymphoma) in the L2 (benign) category. The ROM in the L1 category was 58.3%, in the L2 category- 20.5%, in the L3 category- 57.1%, in the L4 category- 92.6% and in the L5 category- 100%. The diagnostic performance of lymph node fine-needle aspiration biopsy (FNAB) was evaluated by calculating sensitivity (98,1%), specificity (82,7%), positive predictive value (74,5%), negative predictive value (98,9%), and accuracy (87,9%).

Discussion: We believe that the Sydney classification for reporting FNAB improves the quality of the procedure, understanding of the report, and communication between clinicians and cytopathologists, leading to better patient management.

Keywords

Lymph Node Aspiration, Biopsy, Fine-Needle, Sydney Classification

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Introduction

Fine-needle aspiration biopsy (FNAB) is the most common method routinely used in the evaluation of the lymph node. In addition to being a fast, inexpensive and less invasive method, it is also advantageous to obtain material for additional studies such as a cell block for flow cytometry and immunohistochemistry [1, 2]. Despite such advantages, the diagnosis of especially malignant lymphadenopathies (LAP) is largely based on biopsy. However, the diagnosis of benign LAPs can be made with FNAB by using additional studies and unnecessary more invasive methods can be avoided [3-5].

Despite the aforementioned advantages, aspiration biopsy in lymph nodes has not been routinely and generally accepted by clinicians and pathologists because of the diversity of lesions occurring in the lymph nodes, and the clinical indication for aspiration biopsy differs in different places [6-8]. For these reasons and because there is no standard reporting system for the evaluation of tissues such as the cervix, salivary gland, thyroid and urine, in order to bring standardization in the reporting of lymph node aspirations at the International Congress of Cytology held in Sydney in May 2019, 5 subcategories (L1; Insufficient/non-diagnostic, L2; Benign, L3; Atypia of insignificant/ Lymphoid atypia of insignificant (AUS)/ALUS), L4; Malignancy suspected, L5; the malignant) were introduced [9]. After this date, few studies evaluating the diagnostic utility of classification and risk categorization have been published in the literature.

We aimed to evaluate risk categorization according to the Sydney classification in lymph node aspirations performed in our hospital, which has a large archive.

Material and Methods

Ethical approval and study design

Approval from the Ethics Committee of Adana City Education and Research Hospital, Health Sciences University was obtained (Date: 2023-05-11, No: 2561). The preparations of the patients who had lymph node aspiration and histological diagnosis in Adana Training and Research Hospital between January 2020 and March 2023 were extracted from the archive, and patient information was obtained from the hospital information management system and evaluated retrospectively. Cytological materials were re-evaluated by 2 experienced pathologists and categorized according to the Sydney Classification. The Sydney classification includes initial diagnostic level 5 headings: inadequate/nondiagnostic (L1), benign (L2), atypia of insignificant/lymphoid atypia of insignificant significance (AUS/ALUS) (L3), suspected malignancy (L4), and malignant (L5). The malignancy risk (ROM) was determined for each category in patients who underwent cytology-histology correlation with both cell block and additional studies and post-aspiration biopsy. We assessed the diagnostic performance of the procedure by calculating the sensitivity, specificity, and predictive values. The cases were grouped according to age, gender and localization. Aspirations other than lymph nodes were excluded from the study.

Statistical Analysis

We performed statistical analysis using SPSS software (Chicago, USA) to assess the diagnostic performance of FNAB for predicting malignancy. We reported descriptive data for quantitative and qualitative variables as mean and standard deviation, and frequencies and percentages, respectively

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The results of sociodemographic data, localizations and diagnostic categories of the cases are summarized in Table 1. In this study, lymph node fine needle aspiration biopsies (FNAB) of a total of 315 cases, 74 (23.5%) men and 241 (76.5%) women, were examined. The mean age was 51.54 ± 16.0 years; 168 of 315 cases had a history of previously diagnosed tumors. The most common localizations among the cases were axillary (54,0%), cervical (22,9%), and supraclavicular (13,0%) lymph nodes (Table 1).

Diagnostic Categories

In terms of diagnostic categories, 12 (3.8%) cases were L1 (Nondiagnostic), 122 (38.7%) L2 (Benign), 7 (2.2%) L3 (AUS/ALUS), 27 (8.6%) L4 (Suspicion of Malignancy), and 147 (46.7%) were categorized as L5 (Malignant). Thus, L5 ve L2 were the most frequently used categories (Table 1).

A comparison of the Sydney classification and histopathological evaluation of cases is shown in Table 2. There was discordance in the histopathologic examination of 7 (58.3%) cases (6 with breast carcinoma metastases and 1 with thyroid papillary carcinoma metastasis) in the L1 (Non-diagnostic) category (Figure 1).

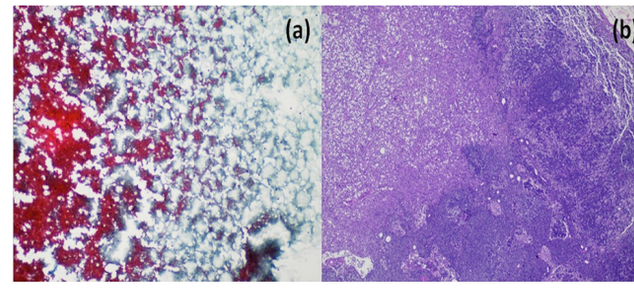

Figure 1. (a). A small number of lymphocytes scattered among the erythrocytes are seen in the smear. (Papanicolaou stain x100). **(b).** Lymph node infiltration with epithelial character cells with large eosinophilic cytoplasm and hyperchromatic nuclei is shown. Tumor cells were immunoreactive for cytokeratin (not shown) (Hematoxylin and Eosin staining X 100).

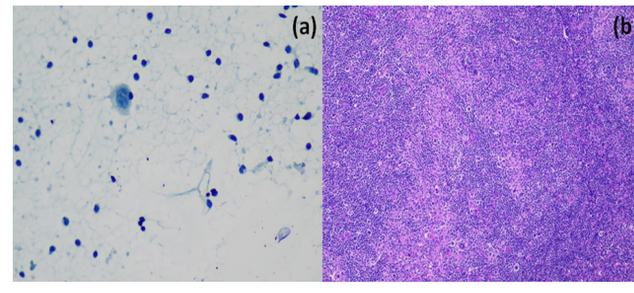

Figure 2. (a). Among the few polymorphic lymphocytes, Reed Sternberg cell with large cytoplasm, binuclear and prominent nucleoli is seen (papanicolau stain x200). **(b).** Histological examination of the lymph node shows scattered Reed Sternberg cells. These cells were positive for CD30 and pale nuclear positive for Pax5 (not shown) (Hematoxylin and Eosin staining X 100).

Table 1. Sociodemographic data, lymph node locations and diagnostic category of the cases

	N, Mean±SD	%, Median (Min-Max)
Gender		
Male	74	23.5
Female	241	76.5
Age (Mean±SD)	51.54±16.0	52.0 (7-90)
History of tumor		
Yes	168	53,4
No	147	46,6
Lymph node locations		
Axillary	170	54.0
Cervical	72	22.9
Supraclavicular	41	13.0
Submandibular	17	5.4
Inguinal	7	2.2
Parotid	5	1.6
Submental	1	0.3
Other	2	0.6
Diagnostic Category		
L1 (Nondiagnostic)	12	3.8
L2 (Benign)	122	38.7
L3 (AUS/ALUS)	7	2.2
L4 (Suspicion of Malignancy)	27	8.6
L5 (Malignant)	147	46.7

AUS/ALUS: atypical cells of undetermined significance/ atypical lymphoid cells of uncertain significance

Table 2. Comparison of the Sydney classification and histopathological evaluation of cases

Sydney Classification	Cytology diagnosis (n=107)	Histopathological diagnosis (n=208)
L1 (Nondiagnostic)	Reagent =5	Breast carcinoma metastasis= 6 Thyroid papillary carcinoma metastasis=1
L2 (Benign)	Reactive lymphoid hyperplasia= 71 Granulomatous lymphadenitis= 15 Chronic lymphadenitis= 6 Other= 5	Hodgkin lymphoma = 12 High grade B-cell lymphoma = 5 breast carcinoma metastasis= 3 Follicular lymphoma= 2 Marginal zone lymphoma= 2 T - acute lymphoblastic lymphoma = 1
L3 (AUS/ALUS)	Reactive lymphoid hyperplasia = 3	Follicular lymphoma=1 Hodgkin lymphoma=1 Small lymphocytic lymphoma=1 T-cell lymphoma=1
L4 (Suspicion of Malignancy)	Chronic lymphadenitis= 2	Hodgkin lymphoma = 7 Thyroid papillary carcinoma metastasis= 4 Breast carcinoma metastasis= 3 Follicular lymphoma= 2 High grade B-cell lymphoma = 2 Other= 7
L5 (Malignant)	-	Breast carcinoma metastasis= 98 Thyroid papillary carcinoma metastasis= 15 Squamous cell carcinoma metastasis= 7 Lung adenocarcinoma metastasis=6 Other= 21

Table 3. Malignancy risk associated with Sydney classification

Sydney classification	Number of	Risk of Malignancy (ROM)	
	Cases	n	%
L1 (Nondiagnostic)	12	7	58.3
L2 (Benign)	122	25	20.May
L3 (AUS/ALUS)	7	4	57.1
L4 (Suspicion of Malignancy)	27	25	92.6
L5 (Malignant)	147	147	100.0

AUS/ALUS: atypical cells of undetermined significance/atypical lymphoid cells of uncertain significance

There was discordance in the histopathologic examination of 25 (20,5%) cases (12 with Hodgkin's lymphoma, 5 with high-grade B-cell lymphoma, 3 with breast carcinoma metastasis, 2 with Follicular lymphoma, 2 with marginal zone lymphoma, and 1 with T-Acute lymphoblastic lymphoma) in the L2 (Benign) category. There was discordance in the histopathologic examination of 4 (57,1%) cases (follicular, Hodgkin, small lymphocytic, and T-cell lymphoma) in the L3 (AUS/ALUS) category (Figure 2). However, there were only 2 (7,4%) benign cases (Chronic lymphadenitis) in the histopathologic examination in the L4 (Suspicion of Malignancy) category. Breast carcinoma metastasis (66.7%) and thyroid papillary carcinoma metastasis (10.2%) comprised the majority of cases in the L5 (malignant) category (Table 2).

Malignancy risk associated with the Sydney classification is shown in Table 3. The most common diagnostic category among the cases was malign. It was found to be 147 (46.7%) in all cases and the ROM rate was 100.0%. There were 122 (38.7%) cases in the L2 (Benign) category and the ROM rate was 20.5%. There were 27 (8.6%) cases in the L4category (Suspicion of Malignancy) and the ROM rate was 92.6%. There were 12 (3.8%) cases in the L1 category (Non-diagnostic) and the ROM rate was 58.3%. There were 7 (2.2%) cases in the L3 category (AUS/ALUS) and the ROM rate was 57.1%. There were 147 (46.7%) cases in the L5 (Malignant) category and the ROM rate was 100.0% (Table 3).

The diagnostic performance of lymph node fine-needle aspiration biopsy (FNAB) was evaluated by calculating sensitivity (98,1%), specificity (82,7%), positive predictive value (74,5%), negative predictive value (98,9%), and accuracy (87,9%).

Discussion

The present study showed the diagnostic accuracy of the Sydney system in Fine needle aspiration biopsy (FNAB) of lymph node pathologies. FNAB is the most common method routinely used in the evaluation of the lymph node [10, 11]. Despite the advantages of FNAB, Sydney classification was introduced because of the diversity of lesions occurring in the lymph nodes, the clinical indication for aspiration biopsy differs in different places, and there is no standard reporting system such as cervix, salivary gland, thyroid, and urine [9]. In our study, we evaluated the histopathological results and risk of malignancy (ROM) of 315 tissues, mostly axillary, cervical and supraclavicular lymph nodes, with the results of the Syndey classification. In terms of Sydney classification, there were 122 (38.7%) cases that were

L2 (Benign) and the ROM rate was found to be 20.5%. There were 27 (8.6%) cases with L4 (Suspicion of Malignancy) and the ROM rate was found to be 92.6%. There were 12 (3.8%) cases with L1 (Non-diagnostic) and the ROM rate was found to be 58.3%. There were 7 (2.2%) cases with L3 (AUS/ALUS) and the ROM rate was 57.1%. There were 147 (46.7%) cases with L5 (Malignant) and the ROM rate was 100.0%. The diagnostic performance of lymph node fine-needle aspiration biopsy (FNAB) was evaluated by calculating sensitivity (98,1%), specificity (82,7%), positive predictive value (74,5%), negative predictive value (98,9%), and accuracy (87,9%).

In our study, 170 (54.0%) patients had axillary LAP, and 72 (22.9%) patients had cervical LAP. In the study by Pandy et al., 24 (12.3%) patients had axillary LAP and 131 (67.5%) patients had cervical LAP [12]. In the study by Vigliar et al., the lymph node locations were cervical LAP in 45.3% and axillary LAP in 18.3% [13]. In the study by Baruah et al. on 220 cases, the lymph node locations were cervical LAP in 55.8% and axillary LAP in 25.8% [14]. In the study by Gupta et al., 14.0% of patients had axillary LAP and 66.8% of patients had cervical LAP [15]. Contrary to studies in the literature, in our study the number of axillary regions was higher than the cervical region in terms of the lymph node locations.

In our study, 7 smears from the L1 (Non-diagnostic) category were found to be malignant lesions (Breast carcinoma metastasis, thyroid papillary carcinoma metastasis) in the histopathological diagnosis and the ROM was 58.3%. Contrary to our study, Pandy et al. did not report any malignant lesions in the L1 category [12]. Similar to our study, a previous study by Gupta et al. found that 27.1% (ROM) of non-diagnostic lymph node fine-needle aspiration (FNAB) smears were malignant [15]. However, Vigilar et al. reported that ROM was 50% in the L1 category [13]. The ROM in our study was relatively higher than in the studies in the literature.

As predicted, the L2 category (Benign) had the lowest ROM of 20.50% in our study. This result is higher compared to that found by Baruah et al. (5,3%), Vigliar et al. (1.92%), Gupta et al. (11.5%) and Caputo et al. (9.38%) [13-16]. Of the 25 malignant cases evaluated in this category, 22 were Hodgkin lymphoma and 3 were breast carcinoma metastasis. The diagnosis of lymphoid type Hodgkin lymphoma by FNAB is extremely difficult, and similar sampling errors have been observed in other studies in the literature [17, 18].

In our study, the ROM evaluated for the L3 category was 57.1%. The risk of malignancy in our study was similar to that reported by Gupta and Vigliar (66.7% and 58.3%), but higher than that reported by Caputo (28.6%) [13, 15, 16]. Of the 7 smears diagnosed as atypia in histopathological sections in the L3 category, 4 were diagnosed as lymphoma of follicular, Hodgkin, small lymphocytic, and T-cell. In this category, 3 (42,9%) were diagnosed as reactive lymphoid hyperplasia. Vigliar's study had the most discordant cases of large cells due to follicular enlargement of reactive lymph nodes, similar to ours [13].

In our study, the risk of malignancy (ROM) for L4 and L5 categories was high, at 92.6% and 100.0%, respectively. In the research we conducted, we did not include benign smears in the L5 category. When looking at these categories, Baruah et al found a ROM of 87.5% and 95%, while Gupta et al reported a ROM of 88% and 99.6% [14, 15]. Consistent with our research, studies by Pandya et al. and Vigliar et al. also reported full marks of 100% for the L4 and L5 categories. This could be attributed to their extensive application of techniques such as flow cytometry and other ancillary procedures [12, 13]. By implementing diagnostic level 2, which incorporates assistive techniques as per the guidelines of the Sydney system, we can significantly decrease the instances of false negatives [19]. In this study, a benign smear categorized as L3 was a case of reactive lymphoid hyperplasia including a few polymorphic lymphocytes, histiocytes and large immunoblast-like cells with a large number of body macrophages, which clarified Reed-Sternberg cells with large cytoplasm, binuclear and prominent nucleoli was seen. Histological examination of the lymph node showed scattered Reed Sternberg cells. These cells were positive for CD30 and pale nuclear positive for Pax5. In cytological examination, immunoblasts resembling Reed-Sternberg cells can often be observed [20].

In our study, the majority of cases fell into the malignant category, accounting for 46.7%, while the benign category accounted for 38.7% of cases. The studies conducted by Gupta et al. and Vigliar et al. found a higher prevalence of cases in the malignant category, mirroring our findings. However, this contrasts with the research of Baruah et al. and Pandya et al., who reported a higher incidence of cases in the benign category [12, 14]. This is probably because cases commonly encountered in healthcare centers are found in the region where viral infections are highly predominant and benign lymphadenopathies are routinely referred for FNAB.

Our study found that the specificity and sensitivity of diagnosing lymph node smear of FNAB using the Sydney classification were 98.1% and 82.7%, respectively. These results are consistent with the findings of other studies conducted by Cupato A et al., Pandya et al., and Vigilar E et al. In the malignant lesions, the sensitivity of FNAB is unstable and ranges from 74% to 99%. In other studies, it has been reported that core biopsies are more advantageous in the diagnosis of malignant lymph nodes for suspicious lymph node lesions [21, 22].

Limitations

The primary constraints of this study include limited sample size, its retrospective nature, and insufficient histopathological follow-up. Additionally, comprehensive clinical, radiological, and follow-up details were not available for all the cases examined in the study.

Conclusion

The suggested lymph node cytology reporting and classification system from Sydney could contribute to consistency and reliability in cytopathological diagnosis. The application of the Sydney classification in the assessment of FNAB is believed to enhance patient care. This enhancement is achieved by improving the procedure's quality, utilizing the material for diagnostic ancillary testing, comprehending the report, and facilitating communication between the cytopathologist and clinician. This will also aid in providing a reasonably precise malignancy risk assessment for further clinical examination.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some

of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest
The authors declare that there is no conflict of interest.

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